Help in evaluating bone allografts

Second in a series on managing bone allografts.

Bone-graft substitutes in all of their many forms have one purpose—to replicate the “gold standard” for bone repair and healing—the patient’s own bone. Though a patient’s own tissue—an autograft—is the ideal replacement for injured or diseased bone, an autograft may not be feasible. The patient’s bone may not be available or healthy. Retrieving an autograft also causes added pain and recovery time for the patient and consumes additional OR time.

The host of graft materials that have arisen as a substitute for the patient’s own bone are challenging to manage. They can be made from human tissue and cells (allografts), animal tissues (xenografts), synthetics, and combinations.

These bone-graft substitutes come in an array of chips, putties, gels, and other materials with a variety of clinical applications from filling bone voids after a fracture to helping late unions to mend to aiding spinal fusions.

Bone allograft market

Bone-graft substitutes are a large and growing industry, expected to generate $1.5 billion in revenue in 2010, according to the Millennium Research Group (chart).

The most common application is in spinal surgery, accounting for 83% of the use of these grafts in 2009, according to Orthopedic Network News (ONN). About 50% of spinal procedures use a bone graft or bone graft substitute. Other applications are in trauma surgery, joint replacements and revisions, and craniomaxillofacial surgery.

Synthetic bone substitutes (such as Vitoss and Mastergraft) accounted for 54% of hospital spending for bone graft materials in 2008, ONN reports, with demineralized bone matrix (DBM) at 24%, allograft bone at 15%, and other materials, 7%.

Evaluating bone graft substitutes

How can perioperative teams ensure that surgeons have the products they need yet avoid overlapping inventory and unnecessary costs?

In evaluating bone allografts, it’s helpful to know the categories they fall into and their roles in healing. (The color-coded chart on page 12 shows the categories of bone repair options.)

Four components are essential for bone healing:
1. An adequate blood supply.
2. Mesenchymal stem cells (MSCs) and osteoprogenitor cells capable of forming bone (osteogenesis).
3. Biological signaling factors to stimulate MSCs and osteoprogenitor cells to differentiate into bone-forming cells, or osteoblasts (osteoinduction).
4. A scaffold to which bone-forming cells can attach and form new bone (osteocnduction).

**Bone biologic characteristics**

An abbreviated list of characteristics useful in evaluating and managing bone biologics includes:
- biocompatibility
- efficacy
- strength
- safety
- availability
- handling/storage
- cost.

This article focuses on biocompatibility, efficacy, and strength. Ensuring safety in tissue donation and screening was addressed in the October 2010 OR Manager. Tissue processing, product evaluation, and cost will be discussed later in this series.

**Biocompatibility**

The bone allograft must be biocompatible; that is, elicit a minimal immune response from the recipient. If the body recognizes the allograft as foreign, it can “wall off” the implant with fibrous tissue and prevent the graft from integrating with the patient’s own bone.

Allografts that provide a scaffold for bone growth, for example, are typically made of calcium phosphate material. These allografts are biocompatible because bone’s normal structure is made up of inorganic materials and minerals like calcium phosphate.

**Efficacy**

The goal for a bone allograft is to form bone or enhance bone formation, in concert with the body’s own healing response. Four common terms describe the efficacy of allografts:
Repairing bone

Bone-graft substitutes seek to replicate the body’s own healing process, which involves these 3 mechanisms.

1. Osteogenesis
New bone is formed by living bone-forming cells from the patient’s own bone marrow or allogeneic stem cells, which differentiate into osteoprogenitor cells and then into osteoblasts.

2. Osteoinduction
Signals induce stem cells and osteoprogenitor cells to become bone-forming cells (osteoblasts). Growth factors can be supplied by the patient’s surrounding bone or from exogenous growth factors from products like bone morphogenic protein (BMP).

3. Osteoconduction
Bone is formed by osteoblasts that have infiltrated an environment conducive to bone formation. One function of bone grafts is to provide a structural support or scaffold for osteoconduction.

Osteoconductive
Like the patient’s own bone, a biologic that is osteoconductive provides a biocompatible scaffold that allows for cellular migration and vascular ingrowth and eventually can be replaced by the patient’s own bone.

Examples: Allografts (such as chips, struts, or shafts), synthetics (ceramics), collagen.

Osteoinductive
An osteoinductive allograft includes signaling factors that stimulate osteoprogenitor cells to differentiate into bone cells. A material is considered osteoinductive if in laboratory studies it forms bone when placed in a non-bony site, such as muscle.

Examples: DBM (such as powders, putties, or pastes), active bone morphogenic protein (BMP).

Osteogenic
A biologic that is osteogenic has cells capable of forming bone.

Examples: Autografts, fresh osteochondral grafts, the patient’s own bone marrow, or stem cell technology.

Osteopromotive
Osteopromotive is a term used more recently to describe products and tissues that may not fall into one of the conventional categories of efficacy. The term may be applied to newer biologics that aren’t necessarily osteoinductive but promote healing by certain factors that stimulate or enhance bone healing.

Example: Platelet-rich plasma.
**Strength**

Biologics can be structural or nonstructural. A structural allograft, such as a strut or shaft, is used when the graft is needed to maintain a structure and provide support, as in joint reconstruction and spinal fusion.

Nonstructural biologics don’t necessarily maintain a structure but fill a bony void or defect. An example is allograft chips.

**Applications for bone allografts**

Allograft materials are selected according to the surgeon’s desired outcome for the patient. These are some examples of common applications. Materials are often used in combination.

- In cases where a scaffold is needed for structural support, as in spinal surgery, the surgeon may select a graft designed for the structural load that also allows for bony in-growth. Examples are struts or shafts and allograft interbody spacers. Polyether-etherketone (PEEK) can be used as a spinal spacer and is filled with a synthetic or biologic material to enhance healing. PEEK does not remodel the host bone and remains in the body.
- If the graft is being used to fill a void or as a graft extender, as in trauma surgery, the surgeon may use graft material in a powdered or particulate form to provide a nonstructural scaffold that will allow bone to form. Examples are synthetic granules, foams, powders, and allograft cancellous chips.
- If the surgeon needs to enhance the patient’s ability to form bone at the healing site, the graft material can provide a biological stimulant. Examples are putties or pastes containing DBM or BMP.
- If a patient has a complex fracture or multiple comorbidities that might inhibit healing, a surgeon might want to add cells to the fracture site, either by adding bone marrow aspirate from the patient or adding allogeneic mesenchymal stem cells, a new technology.

Surgeons also consider factors that might hinder bone healing, such as the lack of blood supply to a fracture site, bacterial infection, or the complexity of the fracture.

Understanding how bone allograft materials are categorized may help OR teams establish criteria for determining how a new graft material proposed for purchase will meet the needs of the surgeon and how it compares with graft materials already in inventory.

—Heather Brannen, PhD
Senior Product Manager, Musculoskeletal Transplant Foundation

—Pat Patterson
Editor, OR Manager

A chart with screening criteria for tissue donors is posted in the OR Manager Toolbox at www.ormanager.com

This series is a collaboration between OR Manager and the Musculoskeletal Transplant Foundation.